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Does urinary tract infection alter fetal fibronectin vaginal swab results?

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Dear Editor,

Cervicovaginal fluid (CVF) fetal fibronectin (FFN) is a reliable test in asymptomatic high-risk women to help predict preterm birth (PTB). Urinary tract infections (UTI) are a treatable risk-factor for PTB risk. FFN is affected by recent intercourse[1] or bleeding[2], but it is unknown whether FFN results are affected by UTI. We hypothesized that levels of FFN in the CVF increases at the time of a UTI but subsequently recovers following treatment. We performed an exploratory longitudinal prospective study to test this.

We studied consecutive women attending an inner-city Prematurity Surveillance Clinic and audited routine clinical tests. Women were high-risk due to previous history of PTB, late miscarriage, cervical surgery or uterine abnormalities. At each visit women provided a mid-stream urine (MSU) which was dipped, and sent for prompt culture in boric acid containers if nitrite positive, leukocyte >1+, or clinician discretion. Women were analysed if an MSU was sent. FFN was measured at each appropriate visit (18^{+0} to 34^{+6} weeks' gestation[3]).

Women with UTI (cases) were gestational age-matched with up to three controls (±2wks). To isolate the effect of UTI on FFN rather than impending PTB, we excluded women with with PTB <34 weeks (a major confounder to FFN). FFN values at the time of positive dipstick, and those 5 weeks before and after, were compared using random-effects GLS (Generalised Least Squares) regression using STATA 15.0.

Of 394 high-risk women, 112 MSUs were cultured. 70 (62.5%) had no growth, 33 (29.5%) grew contaminants and 9 (8%) grew a causative organism. Of the nine cases, two were excluded due to lack of FFN and one excluded due to delivery <34 weeks' gestation. The FFN of the woman who delivered <34wks rose to 200ng/mL at time of UTI, but recovered to 16ng/mL two weeks later. Six cases were matched to sixteen controls and there were no recurrent UTIs.

FFN appeared to increase over time in the controls, although remaining negative (<50ng/mL). Cases appeared to have higher FFNs at baseline and stepped up at time of infection. UTIs could therefore cause false positive (>50ng/mL) FFNs in women who do not deliver preterm. This, however, was not statistically significant as shown by the wide confidence intervals (Figure 1).

We gathered longitudinal data on 394 high-risk women, but only 2.3% had proven UTIs; suggesting that UTI is not a common concern in this group. This is relevant in the community where GPs may empirically treat a positive dip. There appeared to be an increase in FFN at time of infection, but to demonstrate an effect (3.2x FFN increase) with 80% power, 1400 high-risk women would need to be screened. Given the very low prevalence of UTI in this high-risk group, the size of a trial that would be needed to prove an effect would be challenging.

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